

Stewart (D. D.)

A NEW DIAGNOSTIC SIGN FOR THE EARLY
RECOGNITION OF CARCINOMA OF
THE STOMACH.

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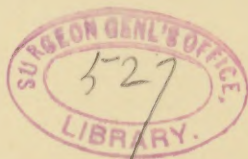
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RECOGNIZING, through some experience in the management of gastric disorders by modern methods of research, the extreme value of data tending to the early diagnosis of malignant disease of the stomach and its separation from affections less grave that often intimately simulate it, it was with great gratification that I read the result of Boas' further investigations as to the significance of a lactic-acid reaction in gastric disease, first mentioned in the second edition of his work on the stomach. In the paper¹ in which the result of his research appears data were given so strongly supporting his earlier assertion, that a marked lactic-acid reaction indicates carcinoma of the stomach, that it was evident the matter merited the serious attention of the clinician.

The utter inability usually to diagnosticate positively a malignant gastric neoplasm in its early

¹ Entitled, "The Occurrence and Diagnostic Value of Lactic Acid in the Stomach," *Münchener medicinische Wochenschrift*, October 24, 1893.



stage, when so situated that the presence of the tumor is undetermined until a period too late for surgical interference, naturally renders one who feels there is no higher court keenly desirous of more certain differentiation-methods than we possess. This is especially felt by the physician, also, on account of the anxiety he must experience in his frequent inability to assert positively that an ailment is not carcinomatous, in the presence of certain forms of gastric disease of insidious and seemingly grave nature, occurring in the middle period of life, of neural or inflammatory origin, the symptomatology and course of which so often intimately suggest a malignant growth.

The early idea that the absence of HCl from the stomach-contents was diagnostic of carcinoma, which arose through the investigation of von den Velden, unfortunately could not be subsequently confirmed, and it is now generally recognized that in a large number of diverse gastric affections, primary or symptomatic, free HCl may be either temporarily or permanently absent. The memory of the once grave import attached to this sign when free HCl was absent for at least a considerable time, in the face of pronounced symptoms, and at an age when the occurrence of carcinoma was possible, and the earlier errors in judgment not infrequently so originated when faith in this indication was strong, should lead one to examine very critically the evidence concerning this new dictum of Boas, which, if true, is so valuable.

With these thoughts in mind I have concerned myself with an examination of the matter since

becoming aware of Boas' earlier results. My desire has been to investigate impartially the subject before saying a word concerning it, and then presenting finally personal evidence *pro* or *con* that could be regarded as conclusive. Unfortunately for my purpose, in the past sixteen months a dearth of that ample and suitable material from which data for conclusive opinion could be finally given, and the too brief time that has elapsed for such positive judgment, do not allow of report now. I regard it essential to direct attention to the subject thus prematurely, however, in order to bring to the notice of the readers of THE MEDICAL NEWS some results of Boas' work, for the purpose especially of correcting a misapprehension that may have been created by some remarks in a paper recently published in these columns, on "The Treatment of Lactic-Acid Excess in the Stomach."¹ In this paper the author, referring very briefly to the result of Boas' valuable investigations, and presumably familiar with the technique employed by the latter, remarks that his own experience entirely negatives Boas' conclusions. He then specifically states that, unlike Boas, he has encountered lactic acid in the stomach, not only during the first part of normal digestion, but also under abnormal conditions, whether these are accompanied by persistent diminution in the secretion of HCl, or in its absence, and in such affections as sluggish motility and gastrectasia, with or without malignant disease, especially when so situated as to cause stenosis.

Although it is evident to me, it cannot be to

¹ By Dr. A. A. Jones.

those not familiar with Boas' work, that the author of this statement has not employed Boas' technique, and is unaware of the very grave errors and utterly useless results that must arise from such inattention, naturally leading to misapprehension and tending to bring the praiseworthy investigations of Boas, from which so much may be expected, into early and undeserved discredit.

The past researches of Ewald and Boas, as is well known, indicated that fermentation lactic acid¹ is regularly formed during the early stage of normal gastric digestion, and that its inhibition and final disappearance occur only in the presence of some amount of unsatisfied free HCl,² and this is still accepted by the many who similarly cling to the ancient idea that lactic acid is a very common accompaniment of the fermentative processes of chronic gastritis and other affections of the stomach, in which there is great diminution in or absence of free HCl. This view was dominant until the recent researches of Martius and Lüttke on HCl-determinations in the stomach, during which these investigators first showed that lactic acid formation does not occur normally in the stomach, as was supposed, and that, moreover, it is absent under conditions in which its presence had been supposed to be quite constant. Previous erroneous results originating the former view have apparently arisen through either trial-meals having been given that contained pre-formed lactic acid or its compounds, or through sources of error not then apparent in the application

¹ As distinct from sarcolactic acid existing in flesh.

² From 0.01 to 0.07 per cent.

of the tests for lactic acid. The results of Martius and Lüttke were so constant as to the evidence of absence of lactic acid both in normal gastric digestion and in chronic gastritis that Boas, in view of these, instituted a reinvestigation of the whole subject. As concerns the former of these points, Boas soon ascertained the highly significant fact, perhaps explanatory of former contrary results and of those of a contrary nature obtained by Dr. Jones,¹ referred to, that *all products of the bakery contain, preformed, an appreciable amount of lactic acid.*²

Adopting a form of trial-meal³ from which error could not arise—a flour-soup, the ethereal extract of which was found not to contain even the minutest traces of lactic acid or lactates—and taking the precaution, first, to cleanse by lavage the stomach in any case in which retarded propulsion would permit remnants of a former meal to be present and falsify the issue, his results have been invariable that not only is lactic acid not present at any stage of normal digestion, whether free HCl be absent or not, but that *it is constantly absent also in all affections of the stomach save carcinoma*. Boas, moreover, found that in the latter lactic acid is usually present

¹ That is, accepting that all sources of error in the application of the tests for lactic acid were eliminated, as is, of course, to be supposed.

² Boas' words are: "Allein es hat sich gezeigt—und das ist ein cardinaler Punkt—dass sämtliche im Handel vorkommenden Gebäckarten mehr oder minder grosse Mengen Milchsäure präformirt enthalten. Alle meine Versuche, mir ein absolut milchsäurefreies Gebäck zu verschaffen, blieben resultatlos."

³ This consisted specifically of a thin gruel made of a tablespoonful of oatmeal flour to the liter of water, and flavored with salt.

during the digestive process in such amounts and at such an early period that by its recognition the ailment may be readily diagnosticated, when other symptoms, such as tumor and increasing cachexia, are yet absent and strong hope exists for a cure by operative means.

Researches in Boas' clinic were made on all types of chronic diseases of the stomach, with the exception of ulcer, in the latter of which Boas naturally regards it as inexpedient either for diagnostic or therapeutic purposes to employ the tube. These cases include a large number of atony, chronic gastritis, pyloric stenosis with consecutive dilatation, and, finally, carcinoma. *In all of these, with the notable exception of the last, even although in the non-malignant cases with pyloric stenosis the trial-meal was allowed to remain over night in the stomach, and marked fermentative processes had occurred, with the presence of sarcinæ, yeast-fungi, hydrogen sulphid, acetone, and the like, lactic acid was always absent.*

In marked contrast to this were the results in the cases of carcinoma. In twenty out of the twenty-one cases studied, whether encountered before the presence of tumor or subsequently, lactic acid was constantly present in such an amount as to give a marked reaction to such a coarse test as that of Uffelmann. In the greater number of these cases there was delayed propulsion, the stomach containing in the morning the remnants of food ingested the evening before. This was especially noted even in the early stage in those cases in which the lesser curvature was afterward shown to be the seat of the growth. In all of the twenty-one cases free HCl

was constantly absent. A strikingly interesting feature that forcibly illustrates the practical diagnostic value of Boas' observations, if further fully confirmed, is the fact that four of these cases came under observation at a very early stage, before any indication of tumor was detectable, and that a diagnosis made by the lactic-acid finding was fully verified by the subsequent development of the characteristic symptoms, including the presence of tumor, and in one of the three, still later, by a necropsy.

This last case is probably that referred to by Cohnheim, of Boas' clinic, in an interesting paper¹ on the early diagnosis of gastric carcinoma. This case is of such striking interest that it merits brief mention here as illustrative of the value of this new diagnostic point.

The patient, a male, forty years old, presented himself at the Polyclinic in Berlin during April, 1892, with symptoms that first led to the diagnosis of gastric ulcer, on which account no examination of the secretory function of the stomach was made. He at first improved on the treatment instituted, and the painful areas, anteriorly and dorsad, suggestive of ulcer, disappeared. Shortly afterward he again returned for treatment, with renewed symptoms, including repeated vomiting. A gastric examination was now made and disclosed absence of free HCl; very pronounced presence of lactic acid, and marked stagnation of the ingesta, but without as yet decided dilatation of the stomach. These findings were obtained with all subsequent—a good number of—tests made. Although no tumor was

¹ Deutsche medicinische Wochenschrift, May 17, 1894.

apparent by the end of May, 1892, Boas diagnosed gastric carcinoma, from the fact of the decided amount of lactic acid always present, the total absence of free HCl, repeated vomiting, decided loss of flesh, and the development of pronounced symptoms of gastric disorder without demonstrable cause.

Under lavage decided improvement occurred, and after two-and-a-half months' treatment the patient was discharged. Two months subsequently (August, 1892) symptoms had recurred, loss in weight continued, and some cachexia had now appeared. The liver was apparently enlarged, yet no tumor was appreciable to palpation. He was again lost sight of, but was finally seen in December, 1892. He then had lost eighty pounds in flesh. The vomit was at times of a "coffee-ground" appearance; there was edema; some swelling of the inguinal glands; fissured, uncoated tongue; a weak, easily compressible pulse. Between the right sternal and parasternal lines, halfway between the xiphoid process and the umbilicus, could now, for the first time, be felt a tumor that seemed to spring from the liver. The stomach was not enlarged to inspection, and no splashing sound was to be obtained. By percussion the greater curvature was found to occupy the umbilical region. The patient shortly afterward died. A necropsy revealed a hard tumor, the size of an apple (an adeno-carcinoma, rich in connective tissue, ulcerated on its mucous surface), occupying the pyloric region and sharply defined from the remainder of the stomach. The pylorus was patent to one finger. The tumor had not been demonstrable to palpation until late in the course of the ailment, because of its being entirely covered by the liver. Resistance in the region of the gall-bladder, which had been felt and which had been regarded as a metastasis to the

liver, had been produced by this tumor so overlapped. This error, considering the unusual position of the growth, was venial.

These results, in the hands of so competent an observer as Boas, very naturally interested me greatly, as my own work lies so largely in a similar field. Although I am as yet unprepared to offer the data I have obtained from an investigation of the subject to the present, because, as remarked, of paucity of material and prematurity of opinion, I may rightly state here that thus far my observations are all in support of Boas, and I have come to feel that much may be expected from this new diagnostic sign.

Apart from its obvious practical positive value, my present experience indicates that it may be regarded of the greatest utility from a negative standpoint, although it is, perhaps, early to speak very positively as to this now. I can at least say that it has stood me in good stead on more than one occasion already. It will be of interest and profit to relate that more than a year ago, when I began routine examinations for lactic acid after Boas' method, and following his technique, I failed to obtain reactions for it in gastric ailments obviously, without this test, not carcinomatous, and I likewise obtained persistently negative results in several cases which then presented, as regards the usual clinical picture, symptoms among not the least of which were loss of weight, more or less cachexia, and a favorable age, strongly suggestive of incipient malignant disease of the stomach. But the continued absence of lactic acid enabled me to take a more

hopeful view, which the sequel has in each case supported.

One of these cases is worthy of notice here. It is that of the mother of one of my former clinical assistants, brought to me in November, 1893, for an opinion because of the gastric ailment being regarded by an earlier attendant as of the nature of possible malignant disease.

The patient, forty-seven years old, who for several years past had had dyspeptic symptoms, developed, somewhat less than a year previously to my seeing her, more or less continuous gastric pain, increased by food often of the plainest sort; there were constipation and vomiting; anorexia was complete, and she had lost much flesh within a few months. This last was apparently largely due to the fact that she had been kept upon a strictly milk diet for a long time. She had frequent attacks, lasting for from some hours to one or two days, in which there was great prostration, with dyspnea, an almost extinct pulse at the wrist, and a very feebly acting heart. When not suffering from these attacks the heart was in fair condition, with a pulse of moderate tension. The patient was highly anemic, somewhat emaciated, with what then seemed a trace of cachexia. The teeth were very imperfect, the breath foul from the latter, and the tongue usually slightly furred. Constant salivation was present. The epigastric area was tender to pressure, slight or deep, and, apparently, more so at the site of the greater curvature and near the pylorus. No evidence of tumor was obtainable. The stomach showed slight dilatation by auscultatory percussion, reaching, when only slightly distended with air and otherwise empty, to within an inch of the umbilicus. The area of liver-dulness was normal; no displacement of the right kidney existed. The urine was free from albumin; urea was normal in amount.

Several gastric examinations made within a few days of each other all showed: Absence of free HCl; no Güinzburg's response until from (variously on different occasions) 0.5 to 2 c.c. of $\text{HCl}_{10}^{\text{N}}$ were added to 10 c.c. of the filtrate. Total acidity, usually from 20 to 30. Digestion-test was but slightly positive in from eight to ten hours, even with the addition of HCl up to 0.2 per cent. free acid. The lab-test was delayed (upward of five hours) in the incubator. The labzymogen-test was positive only at the end of one hour. Gastric propulsion was sluggish; one-and-a-half hours after an Ewald trial-breakfast (a roll and 300 c.c. water) upward of 160 c.c. could be removed. On alternate occasions there were given the baker's-roll breakfast and that of from two-thirds of a pint to a pint of thin gruel. With the former a slight lactic-acid reaction was usually obtained, while with the latter no traces of lactic acid even existed.

Jaworski's test showed no pronounced atrophy of the secretory structure.

Diagnosis: Aggravated chronic gastritis, perhaps originated by the condition of the mouth.

The patient was at once sent to a dentist, and, as her strength permitted, the bad teeth were removed and the mouth put into order.

I instituted a very carefully regulated diet; at first very easily digested, and often of predigested food. Systematic daily lavage was begun, Carlsbad salts were given for constipation, and codein, cannabis indica, and belladonna, for periods of a few days, were used for gastric pain; and the belladonna also to control salivation. At first, for a time, and later for shorter intervals, dilute HCl was administered before meals when predigested food was not given. At the outset it was employed in small, and subsequently in large doses, when nitrogenous

solid food was eaten, as a stimulator of secretion and motility. An active preparation of papain was used after meals. Later, to assist in remedying the anemia, the mixture of iron carbonate was given in teaspoonful-doses after meals, and strychnin and nitro glycerin were employed for the attacks of prostration. Improvement was soon apparent in the subjective symptoms. The appetite returned somewhat. Pain was no longer continuous, but occasionally it was as severe as before; on pressure it had also lessened, and vomiting was less frequent. The tongue soon cleared, and fetor of the breath disappeared, as did finally all tendency to salivation; but at the expiration of four months there was no alteration in the condition of the secretory function of the stomach, although propulsion had slightly improved. Daily lavage could not be continued steadily, because of the exhaustion its practice occasioned, and cascara was substituted for the Carlsbad salts, to remedy the constipation, on account of the salts apparently aggravating the gastric pain. Secretion of free HCl being still lacking after a number of months of the foregoing treatment, intragastric galvanism and faradism were begun and continued in combination, and after several weeks faradism alone for some two months, with still no decided change in secretory function. She was then removed to the seashore. After a few weeks, during which I did not see her, I was informed that although she looked better she still had gastric pain, occasionally vomited, and that on several occasions during morning lavage, while fasting, a little blood and a few particles resembling small pieces of tissue were seen in the water. Unfortunately, these latter had not been saved for examination. When seen later—in August, 1894—her weight was still eight pounds

less than in the winter, probably partly due to change in weight of wearing-apparel. Nothing had been noted in the wash-water for some time. Appetite then was moderate. Epigastric pain and tenderness persisted, but were less in degree than formerly. No tumor was evident and no cachexia. Lactic acid and free HCl were still absent.

This case in several of its features strongly suggested the possibility of one form of latent gastric carcinoma, and had the result of the non detection of lactic acid been contrary, with the coincident steady absence of free HCl under treatment likely to promote its return, I should have regarded it as within the range of probabilities and given a gloomy prognosis. Since the end of summer steady improvement has occurred under the use of full doses of HCl, strychnin, iron, and lavage twice or thrice weekly, and when recently seen the woman presented no indications suggestive of grave disease, although free HCl has not returned.¹ She had regained all the weight lost; had a good color and a good appetite and ate and digested well through the aid of HCl or papain.

The method employed by Boas for the detection of lactic acid in the earlier part of his experiments

¹ An examination after the flour-soup meal at the date of this writing gave the following: One-and-a-half hours after the trial-breakfast, the stomach having been washed the evening before, 100 c.c. were removed by aspiration; the gruel well solved, t. a. = 24; no response to freshly-made Günsburg's solution; no traces of lactic acid. Lab-test positive in one hour; lab-zymogen within one minute. Because of the quantity of filtrate used for the lactic-acid experiment, sufficient was not left for the digestion-test or for examination as to bound HCl.

was the color-test of Uffelmann, so generally used for a like purpose everywhere, because of its simplicity of application and, when certain very important precautions are observed, its accuracy.

A large series of experiments in Boas' clinic convinced him that no color approaching that of the lactic-acid reaction save a *decided* citron-greenish yellow (Cohnheim), or a canary-yellow,¹ could be depended upon; and the fact must be borne in mind that a considerable number of substances react to the ferric-chlorid test in a manner approaching the response of lactic acid, although not so intensely or with the same hue. A differentiation may, therefore, be made by one practically familiar with this color-test. Such substances as acid phosphates, sugar, alcohol, tartaric acid, encountered constantly or occasionally in the stomach-contents, may all mislead the unwary. When this test is employed and a positive reaction is obtained, it is always essential to exhaust a portion of the gastric filtrate with ether, and further test an aqueous solution of the residue. By this means all sources of error, save alcohol, are removed.² Great care must be exercised in the application of such an apparently simple test even as that of Uffelmann or its modifications, and the judgment of none without some practical training in chemic manipulation and acquaintance with the shades of color yielded by varying

¹ Boas speaks of the special hue of these decisive colors as either *saturated canary-yellow* or a *zeissig-yellow*. Any other coloration cannot be regarded as conclusive.

² It must be remembered that all preparations of ether, save that especially obtained without, contain considerable alcohol.

amounts of lactic acid and its simulators is to be depended upon. Especially is this the case when so much hinges upon an opinion in a matter so weighty as the determination of the presence of lactic acid now becomes.

As regards negative results, error may also arise. Ewald speaks of such an observer as Cahn, of Strassburg, who could not at first confirm Ewald's findings as to the presence of lactic acid in the digestion of meat.

The sources of error with Uffelmann's reagent and its lack of delicacy, the inability to depend upon a response unless of the characteristic color mentioned—to produce which its presence in some amount is required—finally led Boas to seek another method that would be of value clinically as well as more exact chemically, and at the same time of far greater delicacy. He finally perfected such a method, which is simple of application, especially when qualitative results only are desired. This method is based upon the fact that when substances containing lactic acid are carefully heated with oxidizers, such as manganese dioxid and sulphuric acid, the lactic acid is decomposed into formic acid and acetic aldehyd. The presence of the last is readily determined by a number of tests. Boas regards the iodoform-test as well suited for both qualitative and quantitative work. By it, the aldehyd conducted into an alkaline solution of iodine forms iodoform. A quantitative examination is possible by this method from the fact that under proper precautions a definite amount of aldehyd decomposes a given quantity of iodine-solution.

Ketone and alcohol, which both react similarly, are readily eliminated by first concentrating the filtrate to be tested to a syrupy consistence. As carbohydrates, similarly treated with oxidizing agents, also yield aldehyd, a watery solution of an ethereal extract¹ of the condensed gastric filtrate, of a non-lactic-acid-yielding trial-meal, must alone be used in the experiment. Special treatment is also required of the filtrate before concentration, should it show the presence of free acids to congo.² As this test properly applied is without sources of error and its manipulation is most easy to one accustomed to chemic work, and it is, moreover, one of great delicacy, it should undoubtedly supplant the old uncertain method of Uffelmann or its modifications.

The scope of this paper—intended merely as a preliminary note and already too lengthy—does not admit of discussion of the most interesting problem as to the cause of the gastric formation of lactic acid only in carcinoma: Whether it be through the production of a lactic-acid enzyme, by the specific agency of the carcinoma, or through the latter alone favoring the abundant development of lactic-acid-generating micro-organisms, probably derived from the mouth, of which more than one variety exists. This question, so interesting and important, will receive due attention in a subsequent paper.

¹ Prepared with an absolutely alcohol-free ether.

² This excellent method I mention here in outline only. The process itself is treated in detail in a paper by Boas in the *Deutsche medicinische Wochenschrift*, September 28, 1893.

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